

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/010198

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K31/519 A61K31/5377 A61K31/541 A61P29/00 A61P31/00
 A61P39/00 A61P3/00 A61P25/28 A61P35/02 A61P1/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
 Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
 EPO-Internal, CHEM ABS Data, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE, SCISEARCH, CANCERLIT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/39129 A (WAER MARK JOSEPH ALBERT ; HERDEWIJN PIET ANDRE MAURITS M (BE); LEUVEN) 6 July 2000 (2000-07-06) page 1, line 1 - page 2, line 10 page 17, line 30 - page 18, line 13 page 19, lines 21-33 compounds 1-3,6,13-16,21-63,65,66 claims 1-6,8,13,14,17 ----- -/--	1-7,9-12

Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *&* document member of the same patent family
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Date of the actual completion of the international search 18 April 2005	Date of mailing of the international search report 26/04/2005
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Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Authorized officer Cielen, E
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PCT/EP2004/010198

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>MATTER HANS ET AL: "Structural requirements for inhibition of the neuronal nitric oxide synthase (NOS-I): 3D-QSAR analysis of 4-oxo- and 4-amino-pteridine-based inhibitors" JOURNAL OF MEDICINAL CHEMISTRY, vol. 45, no. 14, 4 July 2002 (2002-07-04), pages 2923-2941, XP002313348 ISSN: 0022-2623 abstract page 2924, column 1, paragraph 3 page 2924, column 2, paragraph 3 table g; compounds 264,265 tables f,h page 2938, column 1, paragraph 5 page 2938, column 1, paragraph 7 - column 2, paragraph 1</p>	1-12
A	<p>US 5 929 046 A (CAROLA CHRISTOPHE ET AL) 27 July 1999 (1999-07-27) column 1, lines 17-24 column 3, lines 19-57 column 5, lines 32-47 column 6, lines 55-67 page 12, lines 23-32 table Ia; compounds 4290,4316,4288 claims 1,6,15,18,19</p>	1,11,12
X	<p>WO 01/21619 A (PFLEIDERER WOLFGANG ; KOTSONIS PETER (DE); SCHMIDT HARALD (DE); FROEHL) 29 March 2001 (2001-03-29) page 1, lines 10-16 page 4, lines 21-24 page 5, line 1 - page 7, line 10 page 15, lines 11-26 compounds 11-13, 15-39 claims 1-8</p>	1-7,9-12
A	<p>Y. LANDRY, J.-P. GIES: "Pharmacologie. Des cibles vers l'indication thérapeutique. Cours et exercices." 2003, DUNOD, PARIS, XP002313503 page 177, paragraphs 2,3</p>	
A	<p>NICOLAUS B J R: "Symbiotic Approach to Drug Design" DECISION MAKING IN DRUG RESEARCH, XX, XX, 1983, pages 173-186, XP002197412 the whole document</p>	
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PCT/EP2004/010198

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>M.H. BEERS, R. BERKOW: "The Merck Manual of Diagnosis and Therapy, Seventeenth Edition" 1999, MERCK RESEARCH LABORATORIES, WHITEHOUSE STATION, N.J., XP002313611 page 1474, column 1, paragraph 4</p>	9
A	<p>M. H. BEERS, R. BERKOW: "The Merck Manual of Diagnosis and Therapy, Seventeenth Edition" 1999, MERCK RESEARCH LABORATORIES, WHITEHOUSE STATION N.J., XP002313612 page 953, column 2, paragraphs 1,2</p>	9
A	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1992, MOREB JAN ET AL: "The therapeutic potential of interleukin-1 and tumor necrosis factor on hematopoietic stem cells" XP002313613 Database accession no. PREV199395064200 abstract & LEUKEMIA AND LYMPHOMA, vol. 8, no. 4-5, 1992, pages 267-275, ISSN: 1042-8194</p>	1,11
X	<p>WO 03/062240 A (FAUSTUS FORSCHUNGS CIE. TRANSLATIONAL CANCER RESEARCH GMBH; EISENBRAND) 31 July 2003 (2003-07-31) page 1, lines 5-10 page 2, line 20 - page 4, line 17 examples 3,6 claims 1,2</p>	1,6,9-12
X	<p>WO 02/32507 A (ASTRAZENECA AB; BONNERT, ROGER; WALTERS, IAIN) 25 April 2002 (2002-04-25) page 1, lines 3-5 page 1, line 31 - page 3, line 17 page 4, line 30 page 7, line 8 - page 8, line 29 page 9, lines 25-29 example 6 claims 1,15-17</p>	1,8,11,12

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FROELICH LOTHAR G ET AL: "Inhibition of neuronal nitric oxide synthase by 4-amino pteridine derivatives: Structure-activity relationship of antagonists of (6R)-5,6,7,8-tetrahydrobiopterin cofactor" JOURNAL OF MEDICINAL CHEMISTRY, vol. 42, no. 20, 7 October 1999 (1999-10-07), pages 4108-4121, XP002324246 ISSN: 0022-2623 abstract page 4108, column 2, paragraph 1 page 4109, column 1, paragraph 3 table 9 page 4113, column 2, last paragraph - page 4114, column 2, paragraph 3 page 4118, column 2, paragraph 5 - page 4119, column 1, paragraph 2	1-12
X	DD 267 495 A1 (AKADEMIE DER WISSENSCHAFTEN DER DDR,DD) 3 May 1989 (1989-05-03) page 1, paragraph 5 - last paragraph	1,11,12
A	EP 0 362 645 A (THOMAE GMBH DR K) 11 April 1990 (1990-04-11) page 2, lines 11-48 page 3, line 35 - page 4, line 44 page 6, lines 23-30 claims 1,2	1,10-12
A	EP 0 290 819 A (BIORESEARCH SPA; BIORESEARCH S.P.A) 17 November 1988 (1988-11-17) page 2, lines 1-13 table 1; compounds 5,7,8,11 page 4, lines 46-51	1,9-12
A	US 3 122 546 A (OSDENE THOMAS S) 25 February 1964 (1964-02-25) column 1, lines 10-32 column 2, lines 20-35	1
A	EP 0 544 445 A (IMPERIAL CHEMICAL INDUSTRIES PLC) 2 June 1993 (1993-06-02) page 7, lines 7-11 examples 19-21,24,25	1

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 11-12 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4,7-12 (all partially)

Use of a pteridine derivative having the general formula (I), wherein X represents an oxygen atom, for the prevention or treatment of a disorder in a mammal selected from septic or endotoxic shock, TNF-alpha mediated diseases, toxic effects of TNF-alpha and/or anti-cancer chemotherapeutic agents, injuries after irradiation of a tissue of the mammal by radio-elements and cachexia.

Method of prevention or treatment of such disorders comprising administering a pteridine derivative having the general formula (I), wherein X represents an oxygen atom.

2. claims: 1-4, 7-12 (all partially)

Use of a pteridine derivative having the general formula (I), wherein X represents a group with the formula S(O)m, for the prevention or treatment of a disorder in a mammal selected from septic or endotoxic shock, TNF-alpha mediated diseases, toxic effects of TNF-alpha and/or anti-cancer chemotherapeutic agents, injuries after irradiation of a tissue of the mammal by radio-elements and cachexia.

Method of prevention or treatment of such disorders comprising administering a pteridine derivative having the general formula (I), wherein X represents a group with the formula S(O)m.

3. claims: 1-4 (partially), 5-6 (entirely), 7-12 (partially)

Use of a pteridine derivative having the general formula (I), wherein X represents a group with the formula NZ, for the prevention or treatment of a disorder in a mammal selected from septic or endotoxic shock, TNF-alpha mediated diseases, toxic effects of TNF-alpha and/or anti-cancer chemotherapeutic agents, injuries after irradiation of a tissue of the mammal by radio-elements and cachexia.

Method of prevention or treatment of such disorders comprising administering a pteridine derivative having the general formula (I), wherein X represents a group with the formula NZ.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/010198

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0039129	A	06-07-2000	AT 277929 T	15-10-2004
			AU 770551 B2	26-02-2004
			AU 3042900 A	31-07-2000
			CA 2356380 A1	06-07-2000
			DE 69920757 D1	04-11-2004
			WO 0039129 A1	06-07-2000
			EP 1144412 A1	17-10-2001
			JP 2002533464 T	08-10-2002
			US 2004077859 A1	22-04-2004
			US 5929046	A
AU 2014297 A	27-06-1997			
CA 2239968 A1	12-06-1997			
EP 0874848 A1	04-11-1998			
WO 9720843 A1	12-06-1997			
JP 2000501415 T	08-02-2000			
US 6096724 A	01-08-2000			
AT 250060 T	15-10-2003			
AU 697977 B2	22-10-1998			
AU 6805994 A	03-01-1995			
CA 2164847 A1	22-12-1994			
DE 69433161 D1	23-10-2003			
DE 69433161 T2	08-07-2004			
DK 702683 T3	02-02-2004			
EP 0702683 A1	27-03-1996			
FI 955906 A	02-02-1996			
JP 8511773 T	10-12-1996			
NO 954985 A	07-02-1996			
NZ 266527 A	28-10-1999			
PL 311950 A1	18-03-1996			
SK 154795 A3	03-07-1996			
US 6043228 A	28-03-2000			
WO 0121619	A	29-03-2001	DE 19944767 A1	29-03-2001
			AU 7517400 A	24-04-2001
			WO 0121619 A1	29-03-2001
			EP 1216246 A1	26-06-2002
			JP 2004522690 T	29-07-2004
			US 6844343 B1	18-01-2005
WO 03062240	A	31-07-2003	DE 10202468 A1	30-09-2004
			WO 03062240 A1	31-07-2003
			EP 1467994 A1	20-10-2004
			US 2005054653 A1	10-03-2005
WO 0232507	A	25-04-2002	AU 9615101 A	29-04-2002
			EP 1328319 A1	23-07-2003
			JP 2004511532 T	15-04-2004
			WO 0232507 A1	25-04-2002
			US 2004102447 A1	27-05-2004
DD 267495	A1	03-05-1989	NONE	
EP 0362645	A	11-04-1990	DE 3833393 A1	05-04-1990
			AT 106728 T	15-06-1994
			AU 620645 B2	20-02-1992
			AU 4174989 A	05-04-1990
			DD 299062 A5	26-03-1992

INTERNATIONAL SEARCH REPORT
Information on patent family members

International Application No
PCT/EP2004/010198

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
EP 0362645	A	DE 58907824 D1	14-07-1994	
		DK 480489 A	02-04-1990	
		EP 0362645 A2	11-04-1990	
		ES 2056174 T3	01-10-1994	
		FI 894615 A ,B,	02-04-1990	
		HU 208486 B	29-11-1993	
		HU 52504 A2	28-07-1990	
		IL 91814 A	27-02-1994	
		JP 2256676 A	17-10-1990	
		MX 9203034 A1	01-07-1992	
		NO 893879 A ,B,	02-04-1990	
		NZ 230833 A	28-05-1991	
		PT 91836 A ,B	30-04-1990	
		SU 1720491 A3	15-03-1992	
ZA 8907414 A	26-06-1991			
EP 0290819	A	17-11-1988	IT 1204612 B	10-03-1989
		AT 97808 T	15-12-1993	
		DE 3885933 D1	13-01-1994	
		DE 3885933 T2	14-04-1994	
		EP 0290819 A2	17-11-1988	
		ES 2061543 T3	16-12-1994	
		JP 2621925 B2	18-06-1997	
		JP 63297326 A	05-12-1988	
		US 5047405 A	10-09-1991	
US 3122546	A	25-02-1964	NONE	
EP 0544445	A	02-06-1993	CA 2082333 A1	26-05-1993
		EP 0544445 A2	02-06-1993	
		JP 6157540 A	03-06-1994	
		US 5500428 A	19-03-1996	
		US 5300509 A	05-04-1994	